Journal of Saudi Chemical Society (2016) **20**, 651–660

King Saud University

Journal of Saudi Chemical Society

www.ksu.edu.sa
www.sciencedirect.com

ORIGINAL ARTICLE

Synthesis, spectral and biological studies of copper (II) and iron (III) complexes derived from 2-acetyl benzofuran semicarbazone and 2-acetyl benzofuran thiosemicarbazone

Sanjay Goel [a,1], **Sulekh Chandra** [b,*], **Sudhanshu Dhar Dwivedi** [a,2]

[a] *Department of Chemistry, Government Science & Commerce College, Benazeer, Bhopal 462016, India*
[b] *Department of Chemistry, Zakir Husain Delhi College, University of Delhi, Delhi 110002, India*

Received 23 January 2013; accepted 17 July 2013
Available online 23 July 2013

KEYWORDS

Coumarone;
Antioxidant;
Antibacterial;
DPPH;
Lipid peroxidation;
Radical scavenging

Abstract Metal complexes of general composition $[M(L)_2]X_2$ (where M = Cu(II) and X = Cl^-, NO_3^-) and $[M(L)_2]X_3$ (where M = Fe(III) and X = Cl^-, NO_3^-) were synthesized by the condensation of metal salts with semicarbazone (L^a)/thiosemicarbazone (L^b) derived from 2-acetyl benzofuran. The ligands and metal complexes were characterized by NMR, elemental analysis, molar conductance, magnetic susceptibility measurements, IR, atomic absorption, and electronic spectral studies. On the basis of electronic, molar conductance and infrared spectral studies, the complexes were found to have tetrahedral geometry. The Schiff bases and their metal complexes were tested for their antioxidant, radical scavenging and antibacterial activities.

1. Introduction

Metal ions play an important role in biochemical processes. Many biochemical reactions depend on the presence of metal ions which are the part of coordination complexes. The metal ions function to facilitate or inhibit biochemical reactions. Coordination of metal ions by different ligands changes the reduction–oxidation potentials of a reaction, making it easier or, sometimes, more difficult to take place. The change in redox potential finds diverse applications i.e. transport and storage of oxygen and other essential elements, electron transfer etc. There has been considerable interest in the studies of semicarbazones/thiosemicarbazones due to their unusual coordination modes when bound to metals (Basuli et al., 1998). Moreover, the biological properties of semicarbazones/thiosemicarbazones are related to metal ion coordination (Farrell, 2002). The mechanism of action can involve binding to a metal in vivo or the metal complex may be a vehicle for the activation of ligand. Metal complexes derived from Schiff base

* Corresponding author. Tel.: +91 09811226273.
E-mail addresses: sanjaygoelvpci@rediffmail.com (S. Goel), schandra_00@yahoo.com (S. Chandra), sudhanshu_dhar@yahoo.co.in (S.D. Dwivedi).
[1] Tel.: +91 09891616665.
[2] Tel.: +91 09425007434.
Peer review under responsibility of King Saud University.

Production and hosting by Elsevier

http://dx.doi.org/10.1016/j.jscs.2013.07.005

Table 1 Molar conductance and elemental analysis data.

Ligand/complex	Λ_M	Atomic Mass	Colour	M.P (°C)	Yield (%)	Elemental analysis data (%) found (calculated)			
						M	C	H	N
L^a	–	217	Yellow	224	72	–	59.83(60.82)	4.97(5.10)	19.12 (19.34)
$[Cu(L^a)_2](Cl)_2$	178	569	Grey	220	81	11.45(11.17)	46.53(46.45)	3.92(3.90)	14.84 (14.77)
$[Cu(L^a)_2](NO_3)_2$	186	622	Red	223	79	10.13(10.22)	42.64(42.48)	3.62(3.57)	17.89 (18.01)
$[Fe(L^a)_2](Cl)_3$	273	597	Yellow	226	70	9.82(9.95)	47.19(47.08)	3.82(3.95)	15.07 (14.98)
$[Fe(L^a)_2](NO_3)_3$	293	676	Pink	222	76	8.37(8.26)	39.23(39.07)	3.32(3.28)	18.74 (18.64)
L^b	–	233	Light yellow	197	70		56.21(56.63)	4.59(4.75)	17.81 (18.01)
$[Cu(L^b)_2](Cl)_2$	173	601	Dark yellow	240	80	10.65(10.57)	44.10(43.96)	3.76(3.69)	14.21 (13.98)
$[Cu(L^b)_2](NO_3)_2$	191	654	Black	218	76	9.85(9.71)	40.46(40.39)	3.45(3.39)	17.42 (17.13)
$[Fe(L^b)_2](Cl)_3$	268	629	Yellow	220	72	9.01(8.88)	42.24(42.02)	3.63(3.53)	13.53 (13.37)
$[Fe(L^b)_2](NO_3)_3$	289	708	Pink	215	70	8.03(7.88)	37.21(37.30)	3.04(3.13)	17.82 (17.79)

Λ_M: Molar conductance (Ω^{-1} cm^2 mol^{-1}).

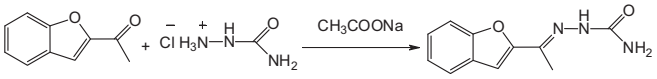
ligands have received considerable attention because they play an essential role in agriculture, pharmaceutical and industrial chemistry (Dhar and Taploo, 1982; Kumar et al., 2009). The formation of variety of metal complexes with Schiff base ligands (Offiong and Martelli, 1997; Casas et al., 2000; Beraldo and Gambino, 2004; Chandra and Gupta, 2005; Joseph et al., 2006; Pelosi, 2010) indicates the spectacular progress in coordination and bioinorganic chemistry. The literature shows that Schiff bases derived from the condensation of benzofuran-2-carbohydrazide with thiophene-2-aldehyde have been synthesized (Ecker et al., 1994; Patil et al., 2010; Halli et al., 2011) and are screened for the antioxidant activity by nitric oxide scavenging potency, H_2O_2 scavenging ability, lipid peroxidation inhibition. In this study we synthesized a new class of copper(II) and iron(III) complexes with newly synthesized Schiff base ligands derived from 2-acetyl benzofuran and studied their importance as antioxidant, DPPH radical scavenger and antibacterial agents in the biological system.

2. Methods

2-Acetyl benzofuran was procured from Sigma–Aldrich. Thiosemicarbazide and semicarbazide are procured from Thomas Baker. All other general chemicals used in the present work were of high purity, Anala R grade and procured from Qualigens and Fluka. Metal salts were purchased from E. Merck and used as received. The solvents used were either spectroscopic pure from SRL/BDH or purified by the recommended methods (Vogel, 1962).

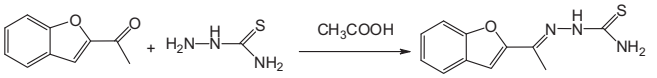
2.1. Synthesis of 2-acetyl benzofuran semicarbazone (L^a)

An aqueous solution of semicarbazide hydrochloride (1.11 g, 0.01 mol, salts are less easily oxidized by air than the free bases and it is in this form that the derivatives of ammonia are best preserved and handled) was added to an ethanolic solution of 2-acetyl benzofuran (1.60 g, 0.01 mol) in the presence of sodium acetate (0.82 g, 0.01 mol). Sodium acetate is added to liberate basic reagent semicarbazide from semicarbazide hydrochloride. The acetic acid formed during the liberation of semicarbazide, protonates the carbonyl oxygen of 2-acetyl benzofuran and makes its carbonyl carbon more susceptible to nucleophilic attack. The reaction mixture was stirred vigorously for 2 h. The completion of the reaction was confirmed by the TLC. The yellow product formed was collected by filtration which was washed several times with hot water and dried in vacuum over P_4O_{10}. The characterization details are tabulated in Table 1.



2.2. Synthesis of 2-acetyl benzofuran thiosemicarbazone (L^b)

A hot ethanolic solution of 2-acetyl benzofuran (1.60 g, 0.01 mol) was mixed with a hot ethanolic solution of thiosemi carbazide (0.91 g, 0.01 mol) in the presence of 0.5 mL acetic acid. Acetic acid is required to protonate carbonyl oxygen of 2-acetyl benzofuran and thus to make its carbonyl carbon more susceptible to nucleophilic attack. For addition reaction, the solution must be acidic enough for an appropriate fraction of the carbonyl compound to be protonated, but not so acidic that the concentration of the base semicarbazide (which may also undergo protonation) becomes too low. The contents were refluxed at 70–80 °C for about 3–4 h. The completion of the reaction was confirmed by the TLC. The solvent was removed using a rotary evaporator and light yellow coloured solid was obtained. It was washed with cold ethanol and dried under vacuum over P_4O_{10}. The characterization details are tabulated in Table 1.



2.3. Preparation of metal complexes

Hot ethanolic solution of metal salts (1 mmol) e.g. $CuCl_2.2H_2O$, $Cu(NO_3)_2.2H_2O$, $FeCl_3$ or $Fe(NO_3)_3$ were mixed with hot ethanolic solution of the ligand e.g. L^a or L^b (2 mmol for copper complexes and 3 mmol for iron complexes). The mixture was refluxed for 4–5 h at 70–80 °C. On cooling the contents, the complex separated out in each case. It was filtered, washed with 50% ethanol and dried under vacuum over P_4O_{10}. The characterization details are tabulated in Table 1.

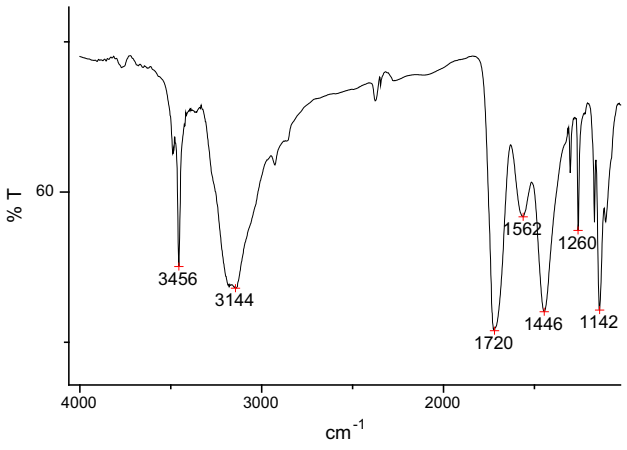


Figure 1 IR Spectra of L^a.

2.4. Physical measurements

The C, H, and N were analysed on a Carlo-Erba 1106 elemental analyser. Metal contents were determined by Atomic Absorption studies. Molar conductance was measured on an ELICO (CM82T) conductivity bridge. Magnetic susceptibilities were measured at room temperature on a Gouy balance using $CuSO_4.5H_2O$ as calibrant. IR spectra (KBr) were recorded on a FTIR spectrum BX-II spectrophotometer. The electronic spectra were recorded in DMSO on a Shimadzu UV mini-1240 spectrophotometer. The ^1H NMR spectra were recorded on a Jeol FT-NMR Spectrometer using DMSO as a solvent. Thermogravimetry (TG) and Differential thermogravimetric (DTA) analysis for the metal complexes were carried out on a Perkin Elmer (Diamond) TG-DTA spectrometer for the determination of complex entrapped water.

3. Results and discussion

3.1. Infrared spectra of L^a

The IR spectrum of ligand L^a (Fig. 1) shows bands at 3456 and 3144 cm^{-1} which may be assigned to [$\upsilon(NH_2)$] and [υ(NH)] groups, respectively. The bands due to [υ(C═O)] which appeared at 1720 cm^{-1} and the bands at 1562 or 1446 cm^{-1} may be assigned to symmetric or asymmetric [υ(C═N)] group (Chandra and Gupta, 2005; Kothari and Sharma, 2011).

3.2. The ^1H NMR spectra of L^a

The ^1H NMR spectrum of the ligand L^a (Fig. 2) was recorded in DMSO. It shows signals at δ 2.21 ppm (s, 3H, –CH_3–C), δ 6.52 ppm (s, 2H, –NH_2–CO), – 9.62 ppm (s, 1H, –N–NH–CO), δ 7.36 ppm (s, 1H, -Ph–CH–C), δ 7.62 (d, J = 7.32, 1H, -Ph), δ 7.57 ppm (d, J = 8.05, 1H, -Ph), δ 7.32 (m, J = 7.33 and 8.05, 1H, -Ph) and δ 7.25 ppm (m, J = 7.32 and 7.33, 1H, -Ph).

3.3. Infrared spectra of L^b

The IR spectrum of the ligand L^b (Fig. 3) shows bands at 3310 and 3148 cm^{-1} which may be assigned to [$\upsilon(NH_2)$] and [υ(NH)] groups respectively. The bands due to [υ(C═S)] appeared at

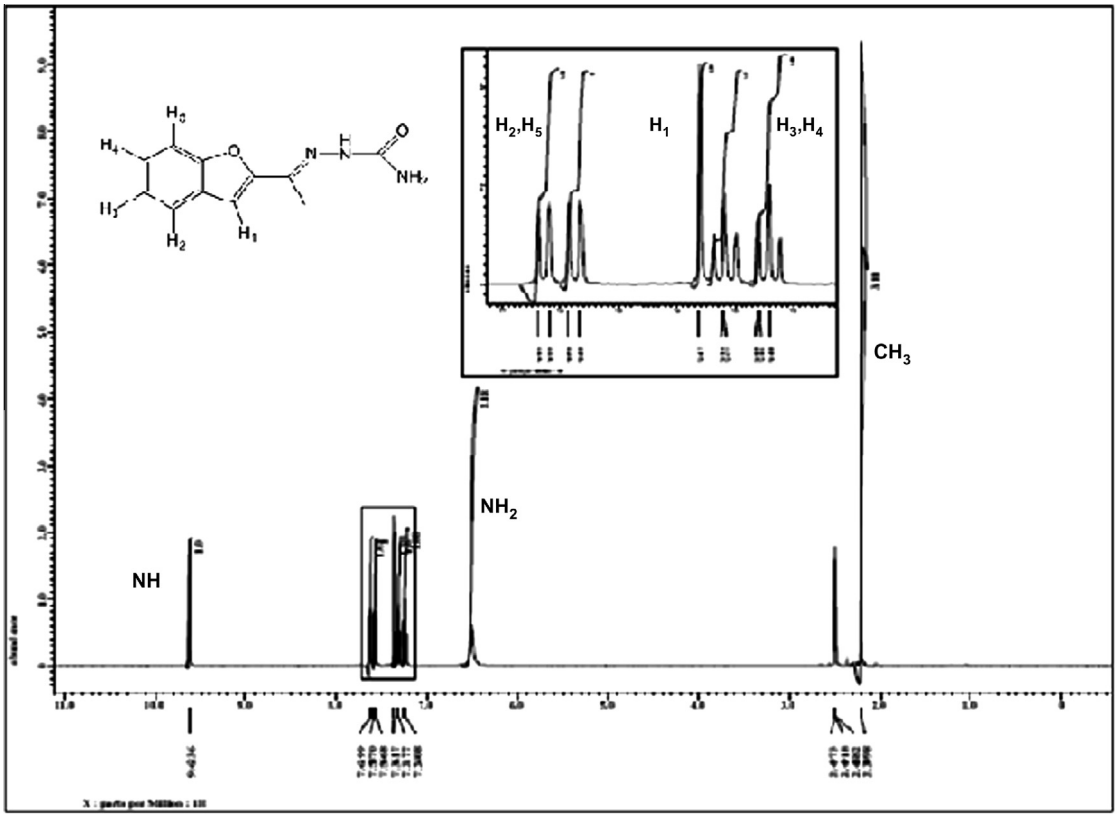


Figure 2 NMR spectra of L^a.

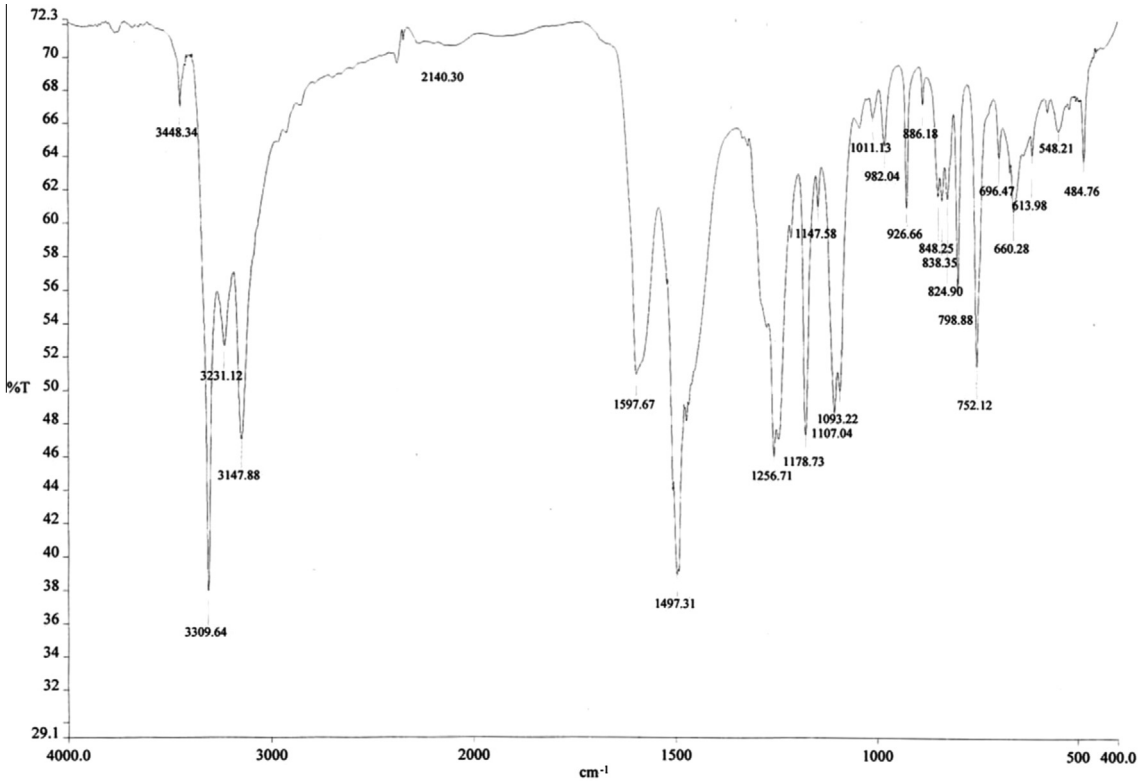


Figure 3 IR Spectra of L^b.

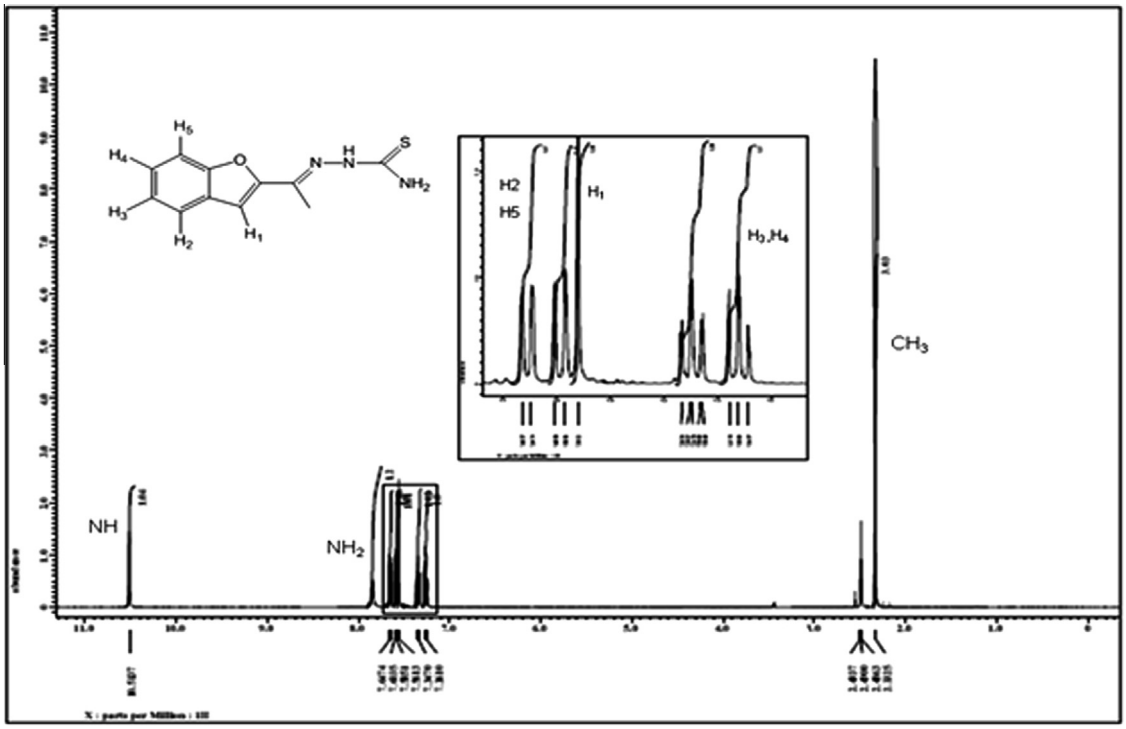


Figure 4 NMR spectra of L^b.

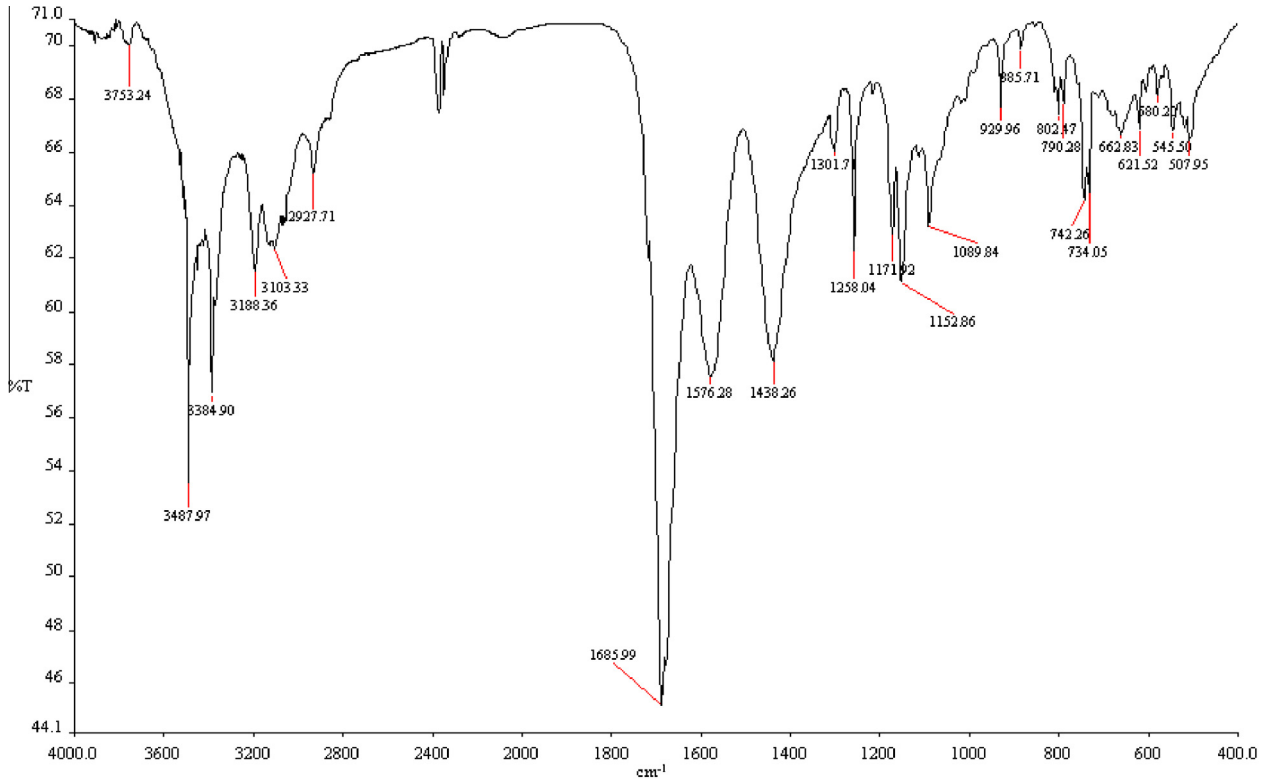


Figure 5 IR Spectra of $[Cu(L^a)_2](Cl)_2$.

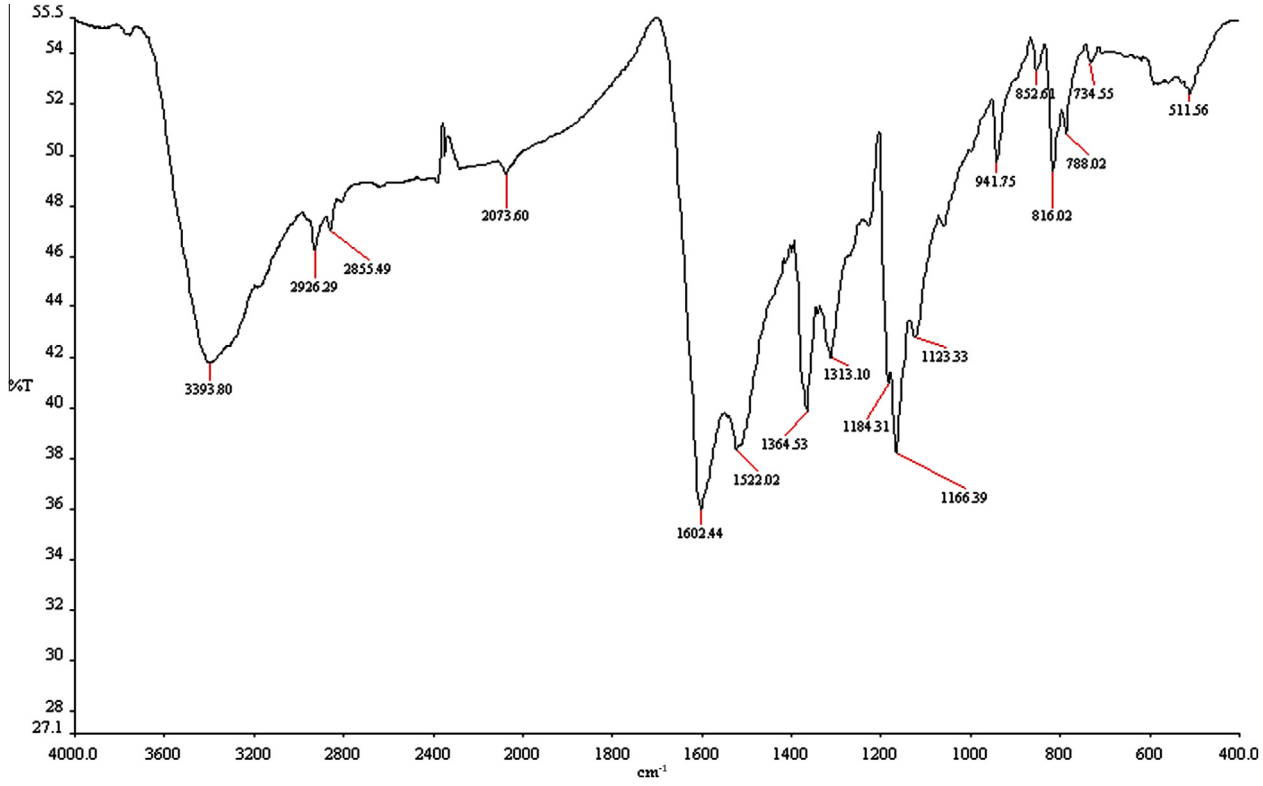


Figure 6 IR Spectra of $[Cu(L^b)_2](Cl)_2$.

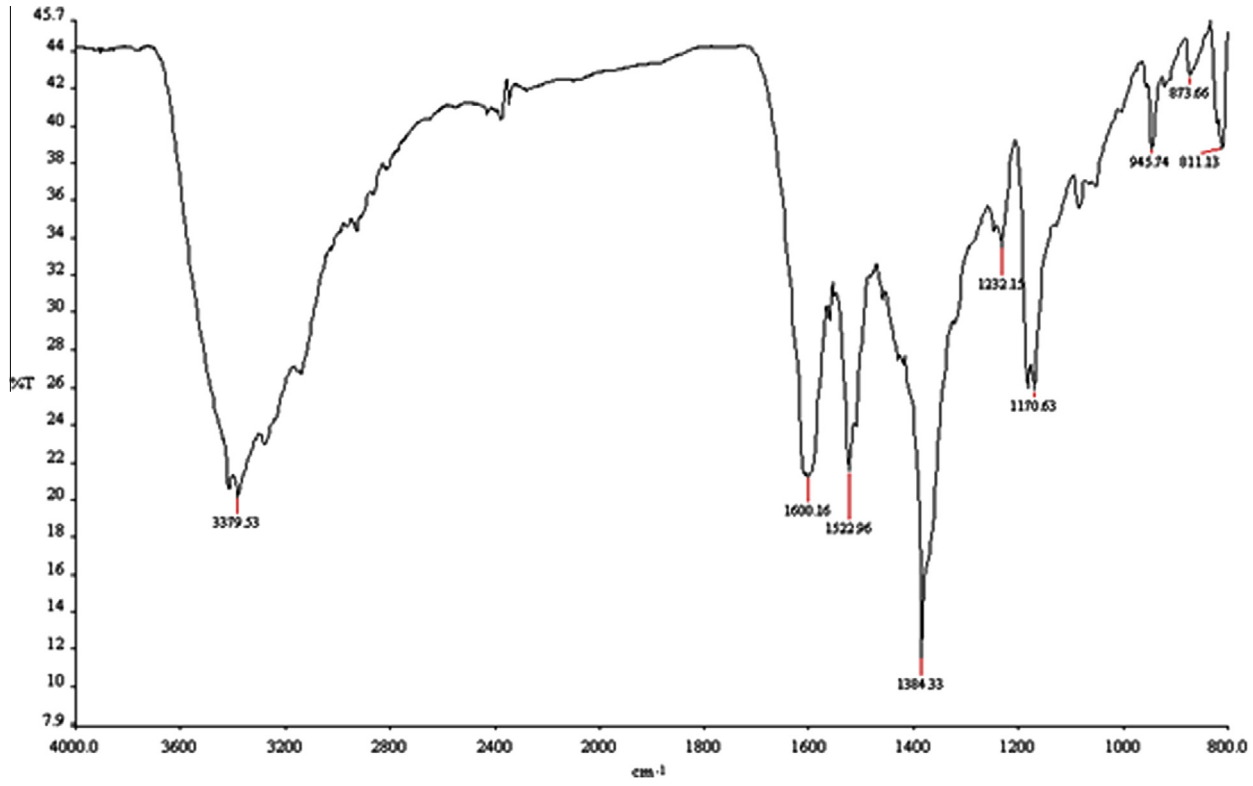


Figure 7 IR Spectra of $[Fe(L^b)_2](NO_3)_3$.

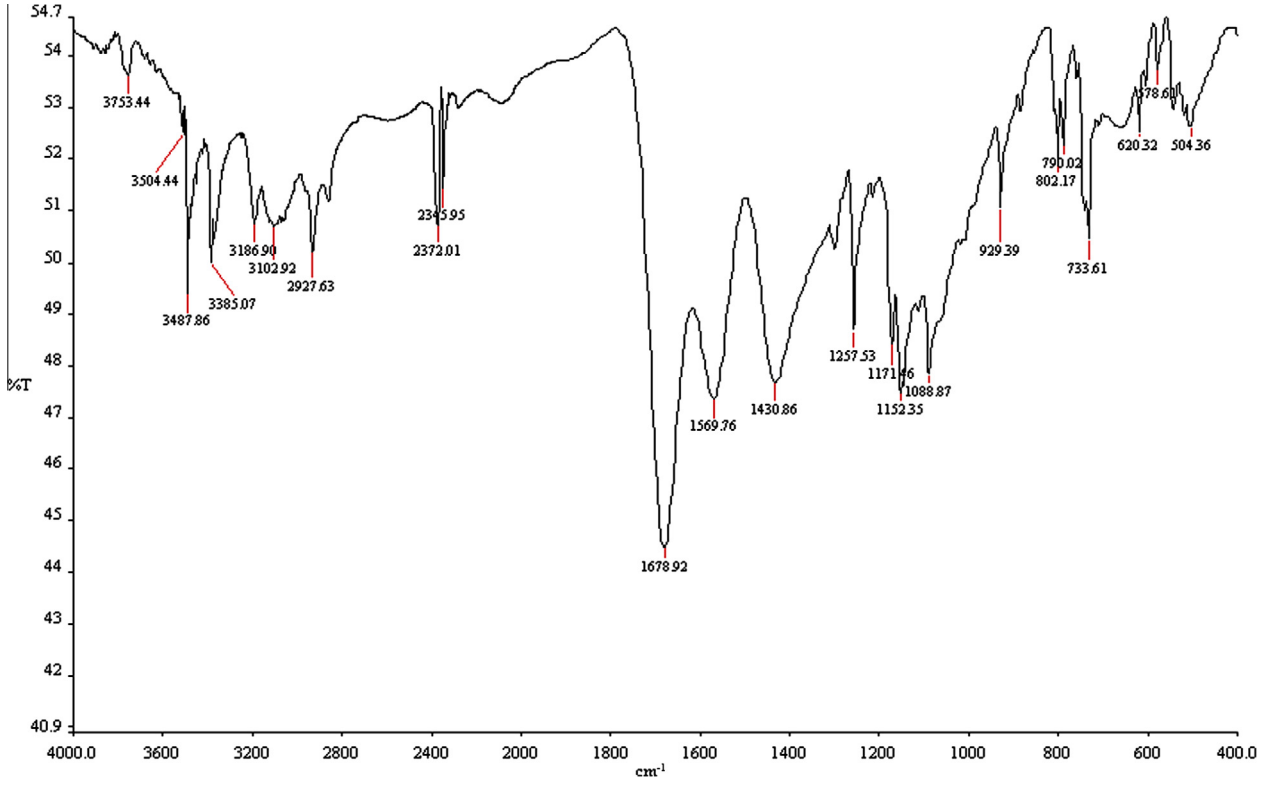


Figure 8 IR Spectra of $[Fe(L^a)_2](Cl)_3$.

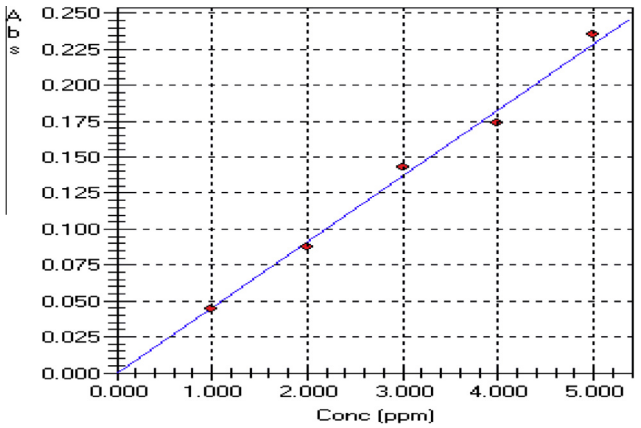


Figure 9 Calibration curve for copper complexes for Atomic Absorption studies. The solution of copper complexes (10 ppm) *i.e.* [Cu $(L^a)_2](Cl)_2$, $[Cu(L^a)_2](NO_3)_2$, $[Cu(L^b)_2](Cl)_2$ and [Cu $(L^b)_2](NO_3)_2$ show the absorbance of 0.0515, 0.0456, 0.0479 and 0.0443 respectively.% of Copper = Absorbance x 10 / Slope (where slope = 0.045).

1598 cm^{-1} and the bands at 1497 or 1257 cm^{-1} may be assigned to symmetric or asymmetric [υ(C═N)] group (Chandra and Gupta, 2005; Kothari and Sharma, 2011).

3.4. The ^1H NMR spectra of L^b

The ^1H NMR spectrum of the ligand L^b (Fig. 4) was recorded in DMSO. It shows signals at δ 2.33 ppm (s, 3H, $–CH_3–C$), δ 7.82 ppm (s, 2H, $–NH_2–CO$), δ 10.51 ppm (s, 1H, –N–NH–CO), δ 7.56 ppm (s, 1H, -Ph–CH–C), δ 7.65 (d, J = 7.32, 1H, -Ph), δ 7.59 ppm (d, J = 7.36, 1H, -Ph), δ 7.35 (m, J = 7.36 and 8.04, 1H, -Ph) and δ 7.26 ppm (m, J = 8.04 and 7.32, 1H, -Ph).

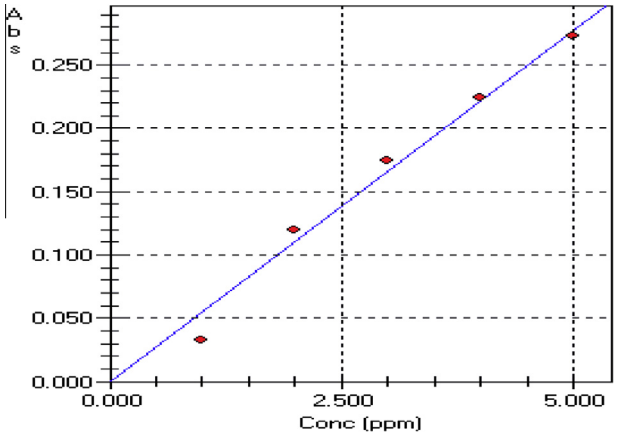


Figure 10 Calibration curve for iron complexes for Atomic Absorption studies. The solution of iron complexes (10 ppm) *i.e.* $[Fe(L^a)_2](Cl)_3$, $[Fe(L^a)_2](NO_3)_3$, $[Fe(L^b)_2](Cl)_3$ and $[Fe(L^b)_2](NO_3)_3$ show the absorbance of 0.0540, 0.0460, 0.0495 and 0.0442 respectively. % of Iron = Absorbance x 10 / Slope (where slope = 0.055).

Table 2 Magnetic moment and Electronic spectral data of complexes.

Complex	μ_{eff}(B.M.)	Electronic spectral data		
		υ_1 (cm^{-1})	υ_2 (cm^{-1})	υ_3 (cm^{-1})
$[Cu(L^a)_2](Cl)_2$	1.98	6631	14580	23450
$[Cu(L^a)_2](NO_3)_2$	2.10	5870	14230	23290
$[Fe(L^a)_2](Cl)_3$	6.09	6697	14109	23281
$[Fe(L^a)_2](NO_3)_3$	6.05	6789	14200	23670
$[Cu(L^b)_2](Cl)_2$	2.03	5889	14980	23560
$[Cu(L^b)_2](NO_3)_2$	2.10	6356	14690	23887
$[Fe(L^b)_2](Cl)_3$	5.95	6732	14230	23450
$[Fe(L^b)_2](NO_3)_3$	6.19	5995	14300	23520

3.5. Infrared spectra of metal complexes

The assignments of the significant IR spectral bands of the metal complexes are shown in Figs. 5–8 which clearly show the shifting of the bands corresponding to υ(–C═N) and υ(–C═S) in thiosemicarbazone or υ(–C═O) in semicarbazone towards the lower side (around ca. 20–50 cm^{-1}) on complexation. This suggests that both the ligands act as bidentate chelating agents coordinating through nitrogen of C═N group and sulphur of C═S group or oxygen of C═O group (Chandra and Gupta, 2005; Kothari and Sharma, 2011).

3.6. Elemental analysis data and molar conductance of metal complexes

The metal contents (Table 1) were determined by the atomic absorption studies as shown in Figs. 9 and 10. The C, H and N contents in the metal complexes were analysed by the elemental analyser and are tabulated in Table 1. The molar conductance measurements (Table 1) of the complexes in DMSO correspond to 1:2 electrolytic nature (Shakir et al., 1993) of copper complexes and 1:3 electrolytic nature of iron complexes. On the basis of elemental analysis data and molar conductance of the complexes, the metal complexes may be formulated as $[ML_2]X_2$ (where M = Cu(II) and X = Cl^-, NO_3^-) and $[ML_2]X_3$ (where M = Fe(III) and X = Cl^-, NO_3^-).

3.7. Magnetic moment and electronic spectral data of metal complexes

At room temperature Cu(II) complexes show magnetic moment in the range 1.98–2.10 B.M corresponding to one unpaired electron (Table 2). They show three electronic spectral bands in the region 5500–7000, 14000–15000 and 23000–24000 cm^{-1} corresponding to the following transitions υ_1: $^2B_1 \rightarrow {}^2A_2$, υ_2: $^2B_1 \rightarrow {}^2A_1$ and υ_3: $^2B_1 \rightarrow {}^2B_2$ indicating the tetrahedral geometry (Chandra and Gupta, 2005; Kothari and Sharma, 2011) of the complexes.

At room temperature Fe(III) complexes show magnetic moment in the range 5.95–6.19 B.M. corresponding to five unpaired electrons (Table 2). They show three electronic spectral bands in the region 5500–7000, 14000–15000 and 23000–24000 cm^{-1} corresponding to the following transitions υ_1: $^6A_1 \rightarrow {}^4T_1$, υ_2: $^6A_1 \rightarrow {}^4A_1$ and υ_3: $^6A_1 \rightarrow {}^4T_2$ indicating

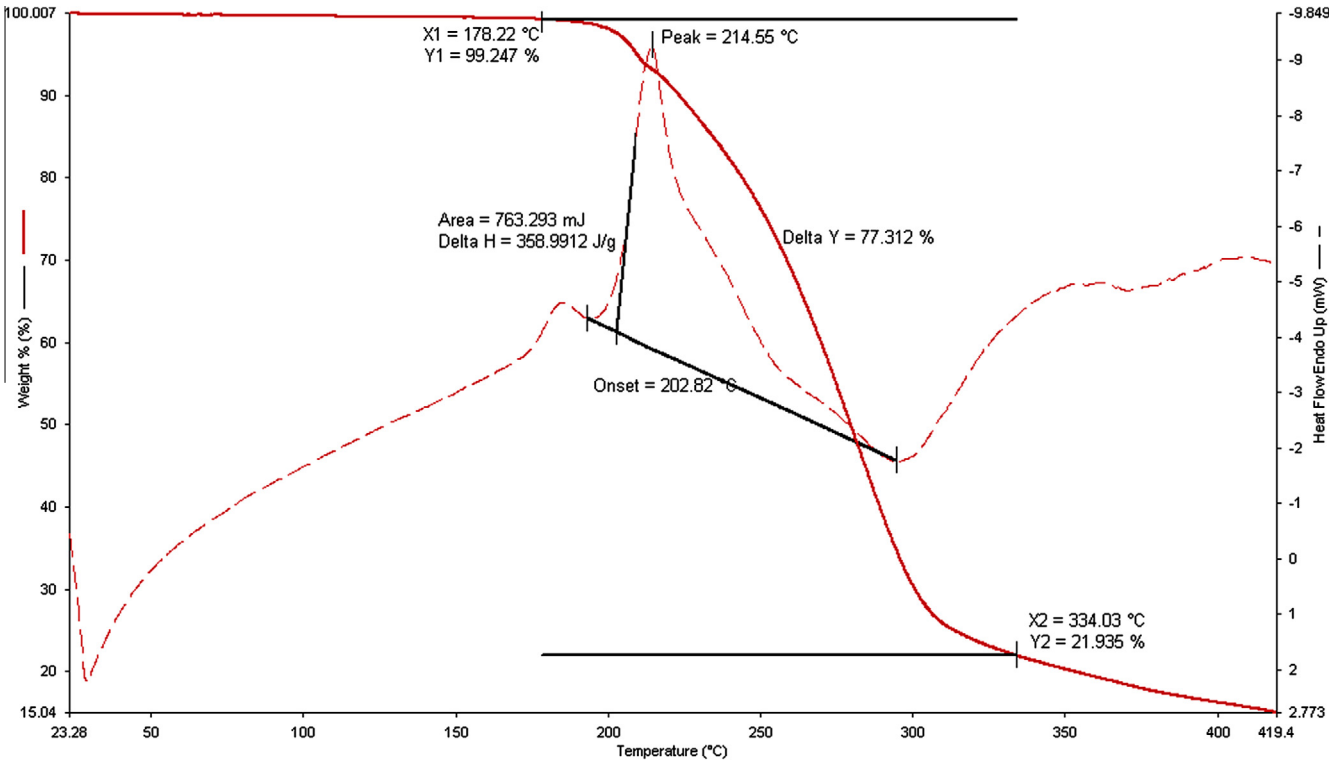


Figure 11 TG-DTA Curve for $[Cu(L^b)_2](Cl)_2$.

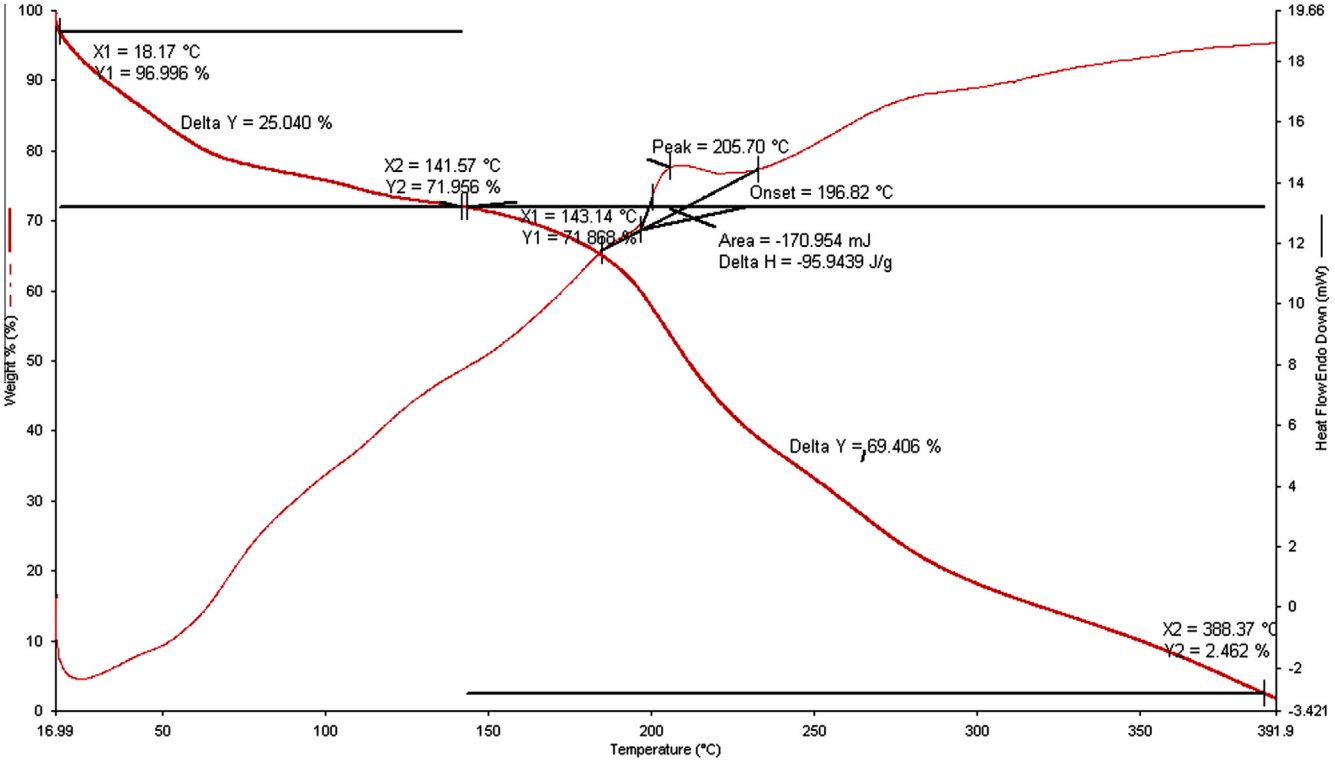


Figure 12 TG-DTA Curve for $[Fe(L^a)_2](NO_3)_2$.

Table 3 Influence of ligands and metal complexes on the initiation of lipid peroxidation.

Ligands/complexes	Percent of control
L^a	98
$[Cu(L^a)_2](Cl)_2$	70
$[Cu(L^a)_2](NO_3)_2$	76
$[Fe(L^a)_2](Cl)_3$	83
$[Fe(L^a)_2](NO_3)_3$	80
L^b	96
$[Cu(L^b)_2](Cl)_2$	64
$[Cu(L^b)_2](NO_3)_2$	61
$[Fe(L^b)_2](Cl)_3$	73
$[Fe(L^b](NO_3)_3$	78

Table 4 Antibacterial activity of ligands and metal complexes.

Test organism	Diameter of zones of inhibition (mm)										
	M_1	M_2	M_3	M_4	M_5	M_6	M_7	M_8	L^a	L^b	K
Escherichia coli	10	10	7	5	15	16	10	9	2	2	22
Klebsiella species	11	11	6	6	17	17	9	9	4	5	20
Shigella sonnei	9	10	8	8	16	15	8	7	3	4	25
Bacillus subtilis	8	10	5	5	15	18	10	8	3	3	23

M_1: $[Cu(L^a)_2](Cl)_2$ M_2: $[Cu(L^a)_2]$ $(NO_3)_2$
M_3: $[Fe(L^a)_2]$ $(Cl)_3$ M_4: $[Fe(L^a)_2](NO_3)_3$
M_5: $[Cu(L^b)_2](Cl)_2$ M_6: $[Cu(L^b)_2](NO_3)_2$
M_7: $[Fe(L^b)_2](Cl)_3$ M_8: $[Fe(L^b)_2](NO_3)_3$
K: Kanamycin

the tetrahedral geometry (Chandra and Gupta, 2005; Kothari and Sharma, 2011) of the complexes.

3.8. TG-DTA data of metal complexes

All the metal complexes show major weight loss above 175 °C which shows that they are free of any entrapped water (Figs. 11 and 12). The peaks due to melting of complexes in TG-DTA curve agree well with the melting point of the complexes (Table 1) as determined by the MP apparatus (Make: BUCHI, Model: M-560).

4. Antioxidant activity

4.1. Assay of initiation of lipid peroxidation

The details of the assay procedure are described in the earlier communication (Raj et al., 1998).The reaction mixture in a final volume of 2 mL consisted of 0.025 M Tris–HCl (pH 7.5), microsomes (1 mg protein) which were taken from the laboratory of Prof. HG Raj, Department of Biochemistry, VP Chest Institute and were prepared by adopting the method of (Ernster and Nordenbrand, 1967) (protein was assayed by the method of Lowry et al., 1951), 3 mM ADP and 0.15 mM $FeCl_3$. The tubes were pre-incubated for 10 min at 37 °C followed by the addition of the test compounds added at a concentration of 100 μM in 0.2 mL of DMSO and then again incubated for 10 min at 37 °C. The reaction was started by the addition of 0.5 mM NADPH for initiation of enzymatic lipid peroxidation and incubated for different intervals. The reaction was terminated by the addition of 0.2 mL of 50% TCA followed by addition of 0.2 mL of 5 N HCl and 1.6 mL of 30% TBA. The tubes were heated in an oil bath at 95 °C for 30 min, cooled and centrifuged at 3000 rpm. The intensity of the colour of the thio barbituric acid reactive substance (TBRS) formed was read at 535 nm. The lipid peroxidation was found to be linear up to 15 min under the conditions described here. The results (Table 3) illustrate the influence of ligands and metal complexes on the initiation of lipid peroxidation enzymatically. These results clearly indicate that metal complexes have higher antioxidant activities as compared to the schiff base ligands. Thiosemicarbazone metal complexes show higher antioxidant activities than semicarbazone metal complexes. Moreover, copper complexes show higher antioxidant activities than iron complexes.

Table 5 DPPH radical Scavenging potency of ligands and metal complexes.

Ligands/Complexes	% of control	Ligands/Complexes	% of control
L^a	97	L^b	94
$[Cu(L^a)_2](Cl)_2$	85	$[Cu(L^b)_2](Cl)_2$	78
$[Cu(L^a)_2](NO_3)_2$	86	$[Cu(L^b)_2](NO_3)_2$	82
$[Fe(L^a)_2](Cl)_3$	85	$[Fe(L^b)_2](Cl)_3$	84
$[Fe(L^a)_2](NO_3)_3$	87	$[Fe(L^b)_2](NO_3)_3$	89

5. Antibacterial activity

The antibacterial activities of the metal complexes were determined at different concentrations (30 μg/disc) against different pathogenic bacteria by using disc diffusion technique and the results were compared with standard antibiotic, Kanamycin (30 μg/disc). It was found that the metal complexes were active against all of the test bacteria but the metal complexes $[Cu(L^b)_2](Cl)_2$ and $[Cu(L^b)_2](NO_3)_2$ were most effective against all pathogenic bacteria as shown in Table 4. Moreover, copper complexes of thiosemicarbazone show remarkable antibacterial activity. The zones of inhibition of the complexes were however lesser as compared to the standard Kanamycin. The metal complexes have higher antibacterial activities as compared to the schiff base ligands. Thiosemicarbazone metal complexes show higher activities than semicarbazone metal complexes.

6. Assay of DPPH radical scavenging

The details of the assay procedure are described as earlier[15]. A solution of test compound (metal complexes/ligands) in methanol (4 mL) at concentration of 100 μM was added to 1 mL of DPPH solution in methanol (0.15 mM). The contents were vigorously mixed, allowed to stand at 20 °C for 30 min and the absorption was read at 517 nm. The effect of the presence of metal complexes/ligands on the rate of the DPPH radical formation is tabulated in Table 5.

7. Conclusions

The present work describes the facile synthesis of metal complexes with newly synthesized Schiff base ligands and their

biological activity. On the basis of elemental analysis data, molar conductance, magnetic susceptibility measurements, IR, mass, atomic absorption and electronic spectral studies, the resulting metal complexes may have tetrahedral geometry and may be formulated as $[M(L)_2]X_2$ (where M = Cu(II) and X = Cl^-, NO_3^-) and $[M(L)_2]X_3$ (where M = Fe(III) and X = Cl^-, NO_3^-) The metal complexes show higher antioxidant, antibacterial activities and radical scavenging potency as compared to the ligands. The copper(II) complexes derived from 2-acetyl benzofuran thiosemicarbazone show remarkable antioxidant and antibacterial activities.

Declaration of Interest

The authors report no declarations of interest.

Acknowledgements

The authors are thankful to the Principal, Zakir Husain Delhi College, Delhi and the Principal, Govt. Science & Commerce College, Benazeer, Bhopal for providing research facilities.

References

Basuli, F., Ruf, M., Pierpont, C.G., Bhattacharya, S., 1998. Unusual coordination mode of thiosemicarbazone ligand: synthesis, structure and redox properties of some ruthenium and osmium complexes. Inorg. Chem. 37 (23), 6113–6116.

Beraldo, H., Gambino, D., 2004. The wide pharmacological versatility of semicarbazones, thiosemicarbazones and their metal complexes. Mini Rev. Med. Chem. 4 (1), 31–39.

Casas, J.S., Garcia, T.M.S., Sordo, J., 2000. Main group metal complexes of semicarbazones and thiosemicarbazones: A structural review. Coord. Chem. Rev. 209 (1), 197–261.

Chandra, S., Gupta, L.K., 2005. Spectroscopic and biological studies on newly synthesized nickel(II) complexes of semicarbazones and thiosemicarbazones. Spectrochim. Acta Part A 62, 1089–1094.

Dhar, D.N., Taploo, C.L., 1982. Schiff bases and their applications. J. Sci. Ind. Res. 41, 501–506.

Ernster, L., Nordenbrand, K., 1967. Assay of initiation of Lipid Peroxidation using thio barbituric acid reactive substance. Methods Enzymol. 10, 574–577.

Ecker, G., Fleischhacker, W., Helml, T., Noe, C.R., Scasny, S., Lemmens-Gruber, R., Studenik, C., Marei, H., Heistracher, P., 1994. Improved synthesis and pharmacologic activity of the enantiomers of a new benzofurane type antiarrhythmic compound. Chirality 6, 329–336.

Farrell, N., 2002. Biomedical uses and applications of inorganic chemistry: An overview. Coord. Chem. Rev. 232, 1–4.

Halli, M.B., Patil, V.B., Sumathi, R.B., 2011. Synthesis, characterization, and biological activity studies of (E)-N'-((thiophen-2-yl)methylene)benzofuran-2-carbohydrazide and its metal(II) complexes. Turk J. Chem. 35, 393–404.

Joseph, M., Sreekanth, A., Suni, V., Kurup, M.R.P., 2006. Spectral characterization of iron(III) complexes of 2-benzoylpyridine N(4)-substituted thiosemicarbazones. Spectrochim. Acta Part A: Molecular and Biomolecular Spectroscopy 64 (3), 637–641.

Kumar, S., Dhar, D.N., Saxena, P.N., 2009. Applications of metal complexes of schiffs bases: A-Review. J. Sci. Ind. Res. 68, 181–187.

Kothari, R., Sharma, B., 2011. Synthesis, Characterization and In-vitro Antimicrobial Investigation of Some Transition Metal Complexes with the Schiff Base of Aromatic Aldehyde. J. Chem. Chem. Sci. 1, 158–163.

Lowry, O.H., Rosenbrough, W.J., Farr, A.L., Randall, R.J., 1951. Protein measurement with the Folin Phenol Reagent. Journal of Biological Chemistry 193, 265–275.

Offiong, O.E., Martelli, S., 1997. Stereochemistry and antitumour activity of platinum metal complexes of 2-acetylpyridine thiosemicarbazones. Trans. Met. Chem. 22 (3), 263–269.

Patil, S.L., Bhalgat, C.M., Burli, S., Chithale, S.K., 2010. Synthesis, Antibacterial and Antioxidant properties of newer 3-(1-benzofuran-2-yl)-5-substituted aryl-1, 2-oxazole. Int. J. Chem. Sci. Appl. 1 (1), 42–49.

Pelosi, G., 2010. Thiosemicarbazone Metal Complexes: From Structure to Activity. Open Crystallogr. J. 3, 16–28.

Raj, H.G., Parmar, V.S., Jain, S.C., Goel, S., Poonam, Himanshu., Olsen, C.E., Wengel, J., 1998. Mechanism of biochemical action of substituted 4-Methylbenzopyran-2-ones. Part 5: Pulse radiolysis studies on the antioxidant action of 7,8-diacetoxy-4-methylcoumarin. Bioorg. Med. Chem. 6, 833–839.

Shakir, M., Varkey, S.P., Hameed, P.S., 1993. Divalent cobalt, nickel, copper and zinc complexes of tetraazamacrocycles bearing polyamide group: Synthesis and characterization. Polyhedron 12, 2775–2780.

Vogel, A.I., 1962. Quantitative inorganic analysis including elemental instrumental analysis, 2nd edition. Longmans Publisher, London.